

Appendix B

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE



In re the application of: Smith, Douglas

Serial No.: 08/487,032

Filed: June 7, 1995

For: NUCLEIC ACID AND AMINO ACID
SEQUENCES RELATING TO HELICOBACTER
PYLORI FOR DIAGNOSTICS AND THERAPEUTICS

Attorney Docket No.: GTN-001

Group Art Unit: 1645

Examiner: V. Portner

Commissioner for Patents
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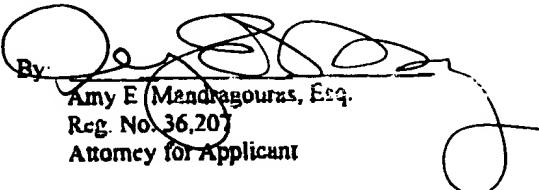
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March 4, 2002

Date of Signature and of Mail Deposit

By:



Amy E. Mandragouras, Esq.
Reg. No. 36,207
Attorney for Applicant

DECLARATION OF DR. PETER C. DOIG PURSUANT TO 37 C.F.R. §1.132

Dear Sir or Madam:

I, Peter C. Doig, hereby declare:

(1) I received my Ph.D. from the University of Toronto in 1990. I am currently a Principal Scientist in the Biochemistry, Infection Discovery Group at AstraZeneca R & D, Boston, MA, where the focus of my research is target based drug discovery efforts in infectious disease. A copy of my curriculum vitae is attached hereto as Exhibit A.

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(2) I have read the specification of the above-referenced patent application (hereinafter the "032 application") and pending claims, as attached hereto as Appendix B. I have also read and understand the relevant portions of the Final Office Action dated February 1, 2001 (Paper No. 32) relating to the Examiner's rejection of the pending claims under 35 U.S.C. §101 and 35 U.S.C. §112, first paragraph, and understand that the Examiner is taking the position that the pending claims lack utility and enablement.

(3) The following studies, which were performed under my direction and supervision, confirm the utility of the claimed isolated polypeptides as having the ability to induce an immune response, as set forth in the '032 application.

(A) Antibodies. Monoclonal antibodies were produced using recombinant histagged HopE (full length mature sequence -11 C-terminal amino acids) or using an outer membrane preparation derived from *H. pylori* strain CCUG 17874. HopE is a 239 amino acid polypeptide which is identical to SEQ ID NO:764 of the '032 application at amino acid residues 24 through 155. Monoclonal antibodies were developed by Immuno-Precise (Victoria B.C., Canada). Polyclonal antibodies were generated in rabbits using Freund's complete adjuvant for the initial priming. Rabbits were given booster immunization in incomplete adjuvant. When antibody titres were sufficient as measured by ELISA (using recombinant HopE as the antigen) and Western blot, animals were sacrificed and sera collected. All work involving animals was performed according to the "Guide for the Care and Use of Laboratory Animals" published by ILAR (The Institute of Laboratory Animal Resources).

(B) Peptide synthesis and epitope mapping. Immobilized overlapping peptides based on the sequence of HopE from J99 were synthesized using the kit purchased from Chiron (mimotope). Peptides were synthesized as 10-mers with an 8-amino acid overlap, with the first peptide starting at the glutamic acid residue of the mature, process protein. ELISA was performed according to the following method. Antigen was fixed to each well by the addition of

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100 μ l antigen solution diluted in carbonate buffer pH 9.6. (10 μ g antigen/ml buffer) and incubate overnight at 4°C. The plate was then washed with TBS (20mM Tris-HCL, 0.9% NaCl pH 7.5) and free sites blocked by incubating 200 μ l of 3% BSA-TBS per well for 1 hour at 37°C. Plates were then washed 3 times with 200 μ l of wash solution (0.05% Tween 20 in TBS) per well. To each well, primary antibody was added (100 μ l) diluted in 0.5% BSA in wash solution, and incubated for 2 h at 37°C. Plates were then washed 3 times with 200 μ l of wash solution per well. To each well, the appropriate secondary antibody (Goat anti rabbit or anti mouse alkaline phosphatase or horse radish peroxidase conjugated) diluted in 0.5% BSA in wash solution was added (100 μ l), and incubated for 2 h at 37°C. The plate was washed three times with wash solution and 100 μ l of substrate was added. For alkaline phosphatase conjugated antibodies, this solution contained 1 mg 4-nitrophenylphosphate/ml in 10 mM diethanolamine pH 9.5- 0.5 mM MgCl₂. The reaction was stopped by the addition of 50 μ l/well of 3 M NaOH and plate read at 410 nm. For horse radish peroxidase conjugated antibodies, either 100 μ l/ well of 0.4 mg OPD/ml in 100 mM citrate buffer, pH 4.5-0.006% H₂O₂ was added, stopped with 50 μ l/well of 4M H₂SO₄ and read at 490 nm or 100 μ l/ well of 0.5 mg ABTS/ml 7 mM phosphate-5 mM citrate buffer pH 4.6-0.015% H₂O₂ was added and read at 410 nm.

(C) **Epitope identification.** Minitope analysis was able to map the epitopes of all monoclonal antibodies examined. The primary peptides that reacted with either monoclonal or polyclonal sera are shown in Table 1, below. These peptides are present in SEQ ID NO:764 of the '032 application.

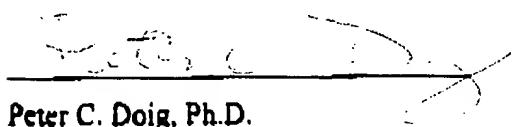
Table 1.

Monoclonal antibody	Type	Epitope
1E8	IgG	QVYAPNPKIQL
3E3	IgG	SVVGCPPGLT
1C10	IgG1	SVVGCPPGLT
1E10	IgG1	SVVGCPPGLT
1F3	IgG1	SVVGCPPGLT

Rabbit Polyclonal		EGDGVYIGTN
Rabbit Polyclonal		DGVYIGTNYQ
Rabbit Polyclonal		VYIGTNYQLG
Rabbit Polyclonal		DCTGSVVGCP
Rabbit Polyclonal		TGSVVQCPPG
Rabbit Polyclonal		SVVGCPPGLT
Rabbit Polyclonal		VGCPPGLTAN
Rabbit Polyclonal		WGVGS DLLAD
Rabbit Polyclonal		VGSDLLADII
Rabbit Polyclonal		SDLLADIIDK

(4) In my opinion, the results of the experiments described herein demonstrate that the claimed polypeptides, including those shown in Table 1 above, have the ability to induce an immune response.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.


Peter C. Doig, Ph.D.

March 1, 2002

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EXHIBIT A**Curriculum Vitae****Peter C. Doig****Current position:**

Principal Scientist,
Biochemistry, Infection Discovery
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Waltham, MA 02451
Tel: (781)-839-4534
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Education: B.Sc., University of Toronto, 1984.
M.Sc., University of Toronto, 1986.
Ph.D., University of Toronto, 1990.

Positions held:

Position	Duties
Principal scientist Biochemistry AstraZeneca R & D Boston (1999-present)	Participate in target based drug discovery efforts in infection discovery in biochemistry. Responsible for protein/enzyme characterization, purification, assay development, and various aspects of lead discovery as well as participating on /leading various drug discovery teams.
Research scientist Biochemistry Astra Research Center Boston (1995-1999)	Participate in/lead teams in identification of Target molecules for therapeutic intervention for <i>H. pylori</i> related disease. Identify and characterize Vaccine candidate antigens from <i>H. pylori</i> .

Research Associate,
Dept. of Biochemistry and Microbiology
University of Victoria (1990-1995)
Supervisor: Dr. T. J. Trust

Identification and characterization of potentially important antigens from the bacterial pathogens *Campylobacter*, *Helicobacter*, and *Aeromonas*.

Scientific Consultant (retainer)
Canadian Bio-Concepts
Victoria, B. C. (1994-1995 (Apr.))

Consultant on the development of various immunological and biosensor reagents.

Scientific Consultant
Micrologix International
Victoria, B. C. (1993)

Consultant on the development of various immuno-diagnostic kits.

Teaching assistant, Microbiology
University of Toronto (1984-1989)

Professional Societies:

American Society for Microbiology

Awards and Fellowships:

Natural Sciences and Engineering Research Council of Canada Post-Doctoral Fellowship (1990, 1991)

Ontario Graduate Fellowship (1989)

Natural Sciences and Engineering Research Council of Canada Postgraduate Fellowship (1986-1988)

University of Toronto Open Scholarship (1984, 1985)

Theses:

M.Sc. Characterization of the binding of *Pseudomonas aeruginosa* alginates to human buccal epithelial cells: structural diversity among alginates.

Ph.D. Characterization of the pilus of *Pseudomonas aeruginosa*: demonstration of an epithelial cell binding domain within the pilin.

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Theses supervisor: R. T. Irvin

Publications:

1. Doig, P., A. L. Franklin, and R. T. Irvin. 1986. The binding of *Pseudomonas aeruginosa* outer membrane ghosts to human buccal epithelial cells. *Can J. Microbiol.* 32:160-166.
2. Doig, P., N. R. Smith, T. Todd, and R. T. Irvin. 1987. Characterization of the binding of *Pseudomonas aeruginosa* alginate to human epithelial cells. *Infect. Immun.* 55:1517-1522.
3. Doig, P., T. Todd, P. A. Sastry, K. K. Lee, R. S. Hedges, W. Paranchych, and R. T. Irvin. 1988. Role of pili in the binding of *Pseudomonas aeruginosa* to human respiratory epithelial cells. *Infect. Immun.* 56:1641-1646.
4. Doig, P., W. Paranchych, P. A. Sastry, and R. T. Irvin. 1989. Human buccal epithelial cell receptors of *Pseudomonas aeruginosa*: identification of glycoproteins with pilus binding activity. *Can. J. Microbiol.* 35:1141-1145.
5. Doig, P., R. Tapping, P. Mankinen-Irvin, and R. T. Irvin. 1989. Effect of microcolony formation on the adherence of *Pseudomonas aeruginosa* to human buccal epithelial cells. *Microbial Ecology Health Dis.* 2:203-209.
6. Irvin, R. T., P. Doig, K. K. Lee, P. A. Sastry, W. Paranchych, T. Todd, and R. S. Hedges. 1989. Characterization of the *Pseudomonas aeruginosa* pilus adhesin: Confirmation that the pilin structural protein subunit contains a human epithelial cell-binding domain. *Infect. Immun.* 57:3720-3726.
7. Lee, K. K., P. Doig, R. T. Irvin, W. Paranchych, and R. S. Hedges. 1989. Mapping the surface regions of *Pseudomonas aeruginosa* PAK pilin: The importance of the C-terminal region for adherence to human buccal epithelial cells. *Mol. Microbiol.* 3:1493-1499.
8. Doig, P., P. A. Sastry, R. S. Hedges, K. K. Lee, W. Paranchych, and R. T. Irvin. 1990. Inhibition of pilus-mediated adhesion of *Pseudomonas aeruginosa* to human buccal epithelial cells by monoclonal antibodies directed against pili. *Infect. Immun.* 58:124-130.
9. Irvin, R. T., P. Doig, P. A. Sastry, B. Heller, and W. Paranchych. 1990. Usefulness of equilibrium parameters of adhesion in predicting outcome of competition for bacterial receptor sites on respiratory epithelial cells by *Pseudomonas aeruginosa* strains of heterologous pilus type. *Microbial Ecology Health Dis.* 3:39-47.
10. Austin, J. W., P. Doig, M. Stewart, and T. J. Trust. 1991. Macromolecular structure and aggregation states of the urease of *Helicobacter pylori*. *J. Bacteriol.* 173:5663-5667.

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11. Trust, T. J., P. Doig, L. Emödy, Z. Kienle, T. Wadström, and P. O'Toole. 1991. High-affinity binding of the basement membrane proteins collagen type IV and laminin to the gastric pathogen *Helicobacter pylori*. *Infect. Immun.* 59:4398-4404.
12. Doig, P., L. Emödy, and T. J. Trust. 1992. Binding of laminin and fibronectin by the major trypsin-resistant structural domain of the crystalline virulence surface array protein of *Aeromonas salmonicida*. *J. Biol Chem.* 267:43-49.
13. Sajjan, U., J. Reisman, P. Doig, R. Irvin, G. Forstner, and J. Forstner. 1992. Interaction of nonmucoid *Pseudomonas aeruginosa* with normal human intestinal mucin and respiratory mucin from patients with cystic fibrosis. *J. Clin. Invest.* 89:657-665.
14. Doig, P., J. W. Austin, M. Kostrzynska, and T. J. Trust. 1992. Production of a conserved adhesin by the human gastroduodenal pathogen *Helicobacter pylori*. *J. Bacteriol.* 174:2539-2547.
15. Austin, J. W., P. Doig, M. Stewart, and T. J. Trust. 1992. Structural comparison of urease and a GroEL analog from *Helicobacter pylori*. *J. Bacteriol.* 174:7470-7473.
16. Collinson, S. K., P. C. Doig, J. L. Doran, S. Cloutier, T. J. Trust, and W. W. Kay. 1993. Thin, aggregative fimbriae mediate binding of *Salmonella enteritidis* to fibronectin. *J. Bacteriol.* 175:12-18.
17. Doig, P., J. W. Austin, and T. J. Trust. 1993. The *Helicobacter pylori* 19.6 kda protein is an iron containing protein resembling ferritin. *J. Bacteriol.* 175:557-560.
18. Doig, P., W. D. McCubbin, C. M. Kay, and T. J. Trust. 1993. Distribution of surface-exposed and non-accessible amino acid sequences among the two major structural domains of the S-layer protein of *Aeromonas salmonicida*. *J. Mol. Biol.* 233:753-765.
19. Doig, P., and T. J. Trust. 1993. Methodological approaches of assessing microbial binding to extracellular matrix proteins. *J. Microbiol. Methods* 18:167-180.
20. Yu, L., K. K. Lee, K. Ens, P. Doig, M. R. Carpenter, R. S. Hedges, R. T. Irvin, and W. Paranchych. 1994. Partial characterization of a *Candida albicans* fimbrial adhesin. *Infect. Immun.* 62:2834-2842.
21. Doig, P. and T. J. Trust. 1994. Identification of surface exposed outer membrane antigens of *Helicobacter pylori*. *Infect. Immun.* 62:4526-4533.
22. Yao, R., H. Niu, P. Doig, T. J. Trust, D. H. Burr, and P. Guerry. 1994. Isolation of motile and non-motile mutants of *Campylobacter jejuni* defective in invasion of eukaryotic cells: role of flagella in invasion. *Mol. Microbiol.* 14:883-894.

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23. Huang, J., P W. O'Toole, P. Doig and T. J. Trust. 1995. Stimulation of interleukin-8 production in cultured epithelial cells by *Helicobacter pylori*. *Infect. Immun.* 63:1732-1738.
24. Exner, M., P. Doig, T. J. Trust, and R. E. W. Hancock. 1995. Identification of a family of outer membrane porins from the gastric pathogen *Helicobacter pylori*. *Infect. Immun.* 63:1567-1572.
25. Doig, P., M. Exner, R. E. W. Hancock, and T. J. Trust. 1995 Isolation and characterization of a conserved 31-kilodalton porin protein from *Helicobacter pylori*. *J. Bacteriol.* 177:5447-5452.
26. Guerry, P., P. Doig, R. A. Alm, D. H. Burr, N. Kinsella, and T. J. Trust. 1996. Identification and characterization of genes required for post-translational modification of *Campylobacter coli* VC167 flagellin. *Mol. Microbiol.* 19:369-378.
27. Doig, P., N. M. Kinsella, P. Guerry, D. H. Burr, and T. J. Trust. Characterization of a post-translational modification of *Campylobacter* flagellin: Identification of a sero-specific glycosyl moiety. *Mol. Microbiol.* 19:379-387.
28. O'Toole, P. W., L. Janzon, P. Doig, J. Huang, M. Kostrzynska , and T. J. Trust. 1995. The putative sialic acid-binding hemagglutinin HpaA of *Helicobacter pylori* CCUG 17874 is a lipoprotein. *J. Bacteriol.* 177: 6049-6057.
29. Doig, P., R. Yao, D. H. Burr, P. Guerry, and T. J. Trust. 1996. An environmentally regulated pilus-like appendage involved in *Campylobacter* pathogenesis. *Mol. Microbiol.* 20:885-894.
30. Alm, R. A., L.-S. Lee, D. T. Moir, B. L. King, E. D. Brown, P. C. Doig, D. R. Smith, B. Noonan, B. C. Guild, B. L. deJonge, G. Carmel, P. J. Tummino, A. Caruso, M. Uria-Nickelsen, D. M. Mills, C. Ives, R. Gibson, D. Merberg, S. D. Mills, Q. Jiang, D. E. Taylor, G. F. Vovis, T. J. Trust. 1999. Genomic-sequence comparison of two unrelated isolates of the human gastric pathogen *Helicobacter pylori*. *Nature* 397:176-180.
31. Doig, P., B. L. de Jonge, R. A. Alm, E. D. Brown, M. Uria-Nickelsen, B. Noonan, S. D. Mills, P. Tummino, G. Carmel, B. C. Guild, D. T. Moir, G. F. Vovis, and T. J. Trust. 1999. *Helicobacter pylori* physiology predicted from genomic comparison of two strains. *Microbiol. Mol. Biol. Rev.* 63:675-707.
32. Alm, R. A., J. Bina, B. M. Andrews, P. Doig, R. E. W. Hancock, and T. J. Trust. 2000. Comparative genomics of *Helicobacter pylori*: Analysis of the outer membrane families. *Infect. Immun.* 68:4155-4168.
33. Ge, Z., P. Doig, and J. G. Fox. 2001. Characterization of proteins in the outer membrane preparation of a murine pathogen, *Helicobacter bilis*. *Infect. Immun.* 69:3502-3506.

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Book Chapters:

Doig, P., P. W. O'Toole, and T. J. Trust. 1997. Molecular characterization of *H. pylori* surface antigens. In *Helicobacter pylori* protocols. Eds. C. L. Clayton and H. T. Mobley. Humana Press Totowa NJ pp. 177-189.

Doig, P. and T. J. Trust. 1997. The molecular basis for *H. pylori* adherence and colonization. In *The immunobiology of *H. pylori*: from pathogenesis to prevention*. Eds. P. B. Ernst, P. Michetti, and P. D. Smith. Lippincott-Raven Publishers, Philadelphia, PA, pp. 47-57.

Invited seminars:

Physiology of *Helicobacter pylori* predicted from the complete genome sequence. Dept. of Gastroenterology, Massachusetts General Hospital, Boston, MA. June, 1999.

Outer membrane components of *Helicobacter pylori*. At IBC's Fourth Annual International Conference on *Helicobacter pylori* and Gastroduodenal Disorders, Washington, D.C. January 27-28, 1997.

Targeting the *Helicobacter pylori* genome: genes to vaccines. At Selected topics in GI disease. Niagara-on-the-Lake, ON, Canada. Nov. 20, 1997.

Abstracts:

Doig, P., and R. T. Irvin. 1985. The adhesion of *Pseudomonas aeruginosa* outer membrane ghosts to human buccal cells. Annual Meeting of the Canadian Society of Microbiologists, Halifax, NS.

Doig, P., N. R. Smith, and R. T. Irvin. 1986. Characterization of the binding of *Pseudomonas aeruginosa* alginate to human buccal epithelial cells. Annual Meeting of the Canadian Society of Microbiologists, Toronto ON.

Doig, P., W. Paranchych, and R. T. Irvin. 1986. The role of pili in the adhesion of *Pseudomonas aeruginosa* K to human buccal epithelial cells. Annual Meeting of the Canadian Society of Microbiologists, Toronto ON.

Paranchych, W., M. Joffe, B. Pasloske, P. A. Sastry, W. Hulbert, P. Mann, P. Doig, R. T. Irvin, and T. Todd. 1987. Adherence factors and *Pseudomonas* colonization of the respiratory tract. North American Cystic Fibrosis Conference, Toronto, ON.

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- Irvin, R. T., T. Todd, P. Doig, and P. M. Mankinen-Irvin.** 1987. The host versus *Pseudomonas aeruginosa* in the pathogenesis of respiratory tract infections. Lister Symposium on Mechanisms of Bacterial Infections. Toronto, ON.
- Doig, P., T. Todd, W. Paranchych, and R. T. Irvin.** 1987. The role of pili in the adhesion of *Pseudomonas aeruginosa* to human respiratory epithelial cells. Annual Meeting of the American Society for Microbiology, Atlanta, GA.
- Doig, P., P. A. Sastry, R. S. Hodges, K. K. Lee, W. Paranchych, and R. T. Irvin.** 1988. Inhibition of adhesion of *Pseudomonas aeruginosa* to human buccal epithelial cells by monoclonal antibodies directed against pili. Annual Meeting of the Canadian Society of Microbiologists, Windsor, ON.
- Saijan, U. S., P. Doig, J. Reisman, R. T. Irvin, G. G. Forstner, and J. F. Forstner.** 1990. Binding of *Pseudomonas aeruginosa* to CF respiratory (RM) and normal intestinal (IM) mucins. Fourth Annual North American & 1990 International CF Conference. Arlington, VA.
- Collinson, S. K., L. Emödy, P. Doig, K-H. Muller, T. J. Trust, and W. W. Kay.** 1991. Aggregative fimbriae of *Salmonella enteritidis*. Canadian Society of Microbiologists 22nd Annual Western Branch Meeting. Vancouver, B. C.
- Austin, J. W., P. Doig, M. Stewart, and T. J. Trust.** 1991. Macromolecular structure of *Helicobacter pylori* urease. Canadian Society of Microbiologists 22nd Annual Western Branch Meeting. Vancouver, B. C.
- Trust, T. J., P. Doig, L. Emödy, Z. Kienle, T. Wadström, and P. O'Toole.** 1991. High-affinity binding of the basement membrane proteins collagen type IV and laminin to the gastric pathogen *Helicobacter pylori*. The IV Workshop of Gastroduodenal Pathology and *Helicobacter pylori*. Bologna, Italy.
- Doig, P., J. W. Austin, and T. J. Trust.** 1991. Identification and characterization of a conserved *Helicobacter pylori* pilus. Sixth International workshop on *Campylobacter*, *Helicobacter*, and related organisms. Sydney, Australia.
- Collinson, S. K., L. Emödy, P. Doig, K-H. Muller, T. J. Trust, and W. W. Kay.** 1992. Binding of tissue matrix proteins to the aggregative fimbriae of *Salmonella enteritidis*. Annual Meeting of the American Society for Microbiology, New Orleans.
- Doig, P. and T. J. Trust.** 1994. Identification of outer membrane surface antigens of *Helicobacter pylori*. Annual Meeting of the Canadian Society of Microbiologists, Vancouver, B. C.
- Doig, P. and T. J. Trust.** 1994. Surface antigens of *Helicobacter pylori*. Annual Meeting of the American Society for Microbiology, Las Vegas.

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Doig, P., M. M. Exner, R. E. W. Hancock, and T. J. Trust. 1995. Identification and characterization of a conserved 31 kilodalton porin protein from *Helicobacter pylori*. 8th International Workshop on Campylobacters, Helicobacters and Related Organisms, Winchester, England.

Doig, P., N. Kinsella, D. H. Burr, P. Guerry, and T. J. Trust. 1995. *Campylobacter* flagellins are post-translationally modified by the addition of a glycosyl moiety. 8th International Workshop on Campylobacters, Helicobacters and Related Organisms, Winchester, England.

Doig, P., J. Cooney, R. Yao, D. Burr, P. Guerry, and T. J. Trust. 1995. Production of pili by *Campylobacter spp.* 8th International Workshop on Campylobacters, Helicobacters and Related Organisms, Winchester, England.

Doig, P., N. Kinsella, P. Guerry, and T. J. Trust. 1995. Characterization of the post-translational modification of *Campylobacter coli* flagellin. Annual Meeting of the American Society for Microbiology, Washington, D. C.

Doig, P., B. Noonan, P. Krishnamurthy, S. Phadnis, N. Vakil, and B. Dunn. 1998. *H. pylori* survives under anaerobic environment and may use H⁺ as terminal electron acceptor. Annual Meeting of the American Gastroenterological Association. New Orleans, LA.

Ge, Z., P. Doig, T. J. Trust, and J. G. Fox. 1999. Characterization of the outer membranes of two murine pathogens, *Helicobacter bilis* and *Helicobacter hepaticus*. Accepted for presentation at the Annual Meeting of the American Gastroenterological Association. Orlando, FL.

Patents:

Title: Synthetic *Pseudomonas aeruginosa* pilin peptide vaccine and method of use.
US patent 5445818, 1995
Inventors: Hodges; R. S., Paranchych; W., Lee; K. K., Parimi; S. A., Irvin; R. T., Doig; P. C.

Title: *Pseudomonas* peptide composition and method.
US patent 5494672, 1996
Inventors: Hodges; R. S., Paranchych; W., Lee; K. K., Parimi; S. A., Irvin; R. T., Doig; P. C., Zouman, D. E., Wong, W. Y.

Title: Synthetic *Pseudomonas aeruginosa* pilin peptide vaccine.
US patent 5612036, 1997
Inventors: Hodges; R. S., Paranchych; W., Lee; K. K., Parimi; S. A.,

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Irvin; R. T., Doig; P. C.

Title: Nucleic acid and amino acid sequences relating to *Helicobacter pylori* and
vaccine compositions thereof.
International application number: PCT/US97/22104